or a mimic thereof is multimeric. Dimeric and multimeric relates to the number of haptoglobin monomers. The haemoglobin may be monomeric or dimeric for each haptoglobin chain.There is a correlation between the type of multimeric forms of the Hp-Hb complex and the degree of binding to a CD163 receptor or a CD163 variant of the invention. A multimeric form of a Hp-Hb complex will due to its size have an increased exposure of encountering CD163 variants as when compared to a monomeric, or even a dimeric form, and thus an increased functional affinity to CD163 variants is observed. Furthermore, the multimeric form of the complex may bind to more than one receptor on the CD163 presenting cell leading to increased avidity of the binding.

The multimers may be created by a common linker moiety, such as S-S bridges as in the naturally occurring haptoglobin. The common linker moiety, is preferably located so that complex-forming with haemoglobin is not disturbed. It is preferred that the common linker moiety is located in the light chain of haptoglobin.

According to the invention the Hp-Hb complex, or a part thereof being operably linked to a substance as described above may be for the use as a medicament. Such medicament may operate through a method, wherein the Hp-Hb complex or a part thereof is used in a method of treatment of an individual, comprising the steps of:

i) providing a Hp-Hb complex, or a part thereof or a mimic thereof capable of binding to the CD163 receptor and/or the CD163 variant,

ii) operably linking a substance as defined above to the Hp-Hb complex or a part thereof or mimic thereof,

iii) administering the medicament comprising the substance operably linked to the Hp-Hb complex to an individual in need thereof.

The term operably linked means that the substance is coupled or bound to the complex in a manner so that the substance is transported to the cell presenting a CD163 receptor or a CD163 variant, whereafter the substance may be released from the complex if appropriate.

Due to the binding of the complex or fragment or mimic thereof to the CD163 receptor and/or a CD163 variant the substance comprised in or bound to the Hp-Hb complex is either taken up by the CD163 presenting cells or at least located in the environment close to the cells. Thereby it is possible to concentrate the substance in or around the cell presenting the CD163 receptor. A test for analysing optional uptake is described below in Example 4.

In one embodiment of the invention the Hp-Hb complex, or a part thereof may be operably linked to a substance, such as a medicament, a gene, a vesicle, vector or the like.

The medicament may be any medicament for which it is desirable to target the drug to a particular tissue or particular cells. In particular the medicament is an antimicrobial agent or a cancer drug.

The medicament is preferably a medicament against diseases in relation to monocytes, such as macrophages. In particular the invention relates to a complex being operably linked to a anti-HIV drug.

In another embodiment the substance is a medicament against lymphomas, such as histiocytic lymphomas.

In yet another embodiment the substance may stimulate the macrophages to produce interleukin 6.

In a further embodiment the substance is an antigen for vaccine purposes.

In another embodiment the substance of the Hp-Hb complex, or a functional equivalent thereof comprises a gene, i.e. a gene construct. The gene may be any gene encoding a particular biological function. For example the gene may comprise a nucleic acid, such as PNA, LNA, DNA or RNA, or the gene may comprise cDNA. The gene may also comprise less than full length genes or cDNAs, such as fragment thereof. The Hp-Hb complex comprising a gene may be used in gene-delivery therapy, whereby the gene is taken up by the cell presenting the CD163 receptor or a variant thereof.

The constructs can be introduced as one or more DNA molecules or constructs. The constructs are prepared in conventional ways, where the genes and regulatory regions may be isolated, as appropriate, ligated, cloned in an appropriate cloning host, analyzed by restriction or sequencing, or other convenient means. Using PCR, individual fragments including all or portions of a functional unit may be isolated, where one or more mutations may be introduced using "primer repair", ligation, in vitro mutagenesis, etc. as appropriate. The construct(s) once completed and demonstrated to have the appropriate sequences may then be introduced into host cells by any convenient means, as discussed in more detail below.

The constructs may be introduced as a single DNA molecule encoding all of the genes, or different DNA molecules having one or more genes. The constructs may be introduced simultaneously or consecutively, each with the same or different markers.

The gene may be linked to the complex as such or protected by any suitable system normally used for transfection such as viral vectors or artificial viral envelope, liposomes or micellas, wherein the system is linked to the complex.

Numerous techniques for introducing DNA into eukaryotic cells are known to the skilled artisan. Often this is done by means of vectors, and often in the form of nucleic acid encapsidated by a (frequently virus-like) proteinaceous coat. Gene delivery systems may be applied to a wide range of clinical as well as experimental applications.

Vectors containing useful elements such as selectable and/or amplifiable markers, promoter/enhancer elements for expression in mammalian, particularly human, cells, and which may be used to prepare stocks of construct DNAs and for carrying out transfections are well known in the art. Many are commercially available.

Various techniques have been developed for modification of target tissue and cells in vivo. A number of virus vectors, discussed below, are known which allow transfection and random integration of the virus into the host. See, for example, Dubensky et al. (1984) Proc. Natl. Acad. Sci. USA 81:7529-7533; Kaneda et al., (1989) Science 243:375-378; Hiebert et al. (1989) Proc. Natl. Acad. Sci. USA 86:3594-3598; Hatzoglu et al., (1990) J. Biol. Chem. 265:17285-17293; Ferry et al. (1991) Proc. Natl. Acad. Sci. USA 88:8377-8381. Routes and modes of administering the vector include injection, e.g intravascularly or intramuscularly, inhalation, or other parenteral administration.

Advantages of adenovirus vectors for human gene therapy include the fact that recombination is rare, no human malignancies are known to be associated with such viruses, the adenovirus genome is double stranded DNA which can be manipulated to accept foreign genes of up to 7.5 kb in size, and live adenovirus is a safe human vaccine organisms.

Another vector which can express the DNA molecule of the present invention, and is useful in gene therapy, particularly in humans, is vaccinia virus, which can be rendered non-replicating (U.S. Pat. Nos. 5,225,336; 5,204,243; 5,155,020; 4,769,330).

Based on the concept of viral mimicry, artificial viral envelopes (AVE) are designed based on the structure and composition of a viral membrane, such as HIV-1 or RSV and used to deliver genes into cells in vitro and in vivo. See, for example, U.S. Pat. No. 5,252,348, Schreier H. et al., J. Mol. Recognit., 1995, 8:59-62; Schreier H et al., J. Biol. Chem., 1994, 269:9090-9098; Schreier, H., Pharm. Acta Helv. 1994, 68:145-159; Chander, R et al. Life Sci., 1992, 50:481-489, which references are hereby incorporated by reference in their entirety. The